An antimicrobial stewardship program reduces antimicrobial therapy duration and hospital stay in surgical wards

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ABSTRACT

We report a quasi-experimental study of the implementation of an antimicrobial stewardship program in two surgical wards, with a pre-intervention period with just assessment of prescription and an intervention period with a prospective audit on antibiotic prescription model. There was a significant reduction of length of stay and the total days of antimicrobial administration. There were no differences in mortality between groups.

The antimicrobial stewardship program led to the early detection of inappropriate empirical antibiotic treatment and was associated with a significant reduction in length of stay and the total duration of antimicrobial therapy.

KEYWORDS: Antimicrobial therapy, Stewardship Program, Length of Stay

Un programa de uso de antimicrobianos reduce la duración de la terapia antimicrobiana y la estancia hospitalaria en salas de cirugía

RESUMEN

Presentamos un estudio cuasi-experimental de la aplicación de un programa de uso de terapia antimicrobiana en dos salas quirúrgicas, con un período de pre-intervención en que se realizó evaluación de la prescripción y un período de intervención con una auditoría prospectiva sobre la prescripción antibiótica siguiendo un modelo de recomendación. Hubo una reducción significativa de la estancia media y del total de días de tratamiento antibiótico. No hubo diferencias en la mortalidad entre los grupos.

El programa de uso de terapia antimicrobiana condujo a la detección precoz de tratamiento antibiótico empírico inadecuado y se asoció con una reducción significativa de la estancia media y la duración total de la terapia antimicrobiana.

Palabras clave: tratamiento antimicrobiano, programa de uso de antimicrobianos, entancia media

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INTRODUCTION

Antimicrobial stewardship programs (ASP) assist in optimizing antimicrobial prescribing in hospitalized patients. They do this by aiding in the selection, dosing and duration of antimicrobial treatment, so enhancing clinical outcomes, minimizing antimicrobial resistance and improving thequality of patient care and safety[1,2].

Many studies of both adults and children have demonstrated the benefits of such ASP[3,4]. The different studies show both positive and negative effects[1,4] and it has therefore been difficult for hospitals, healthcare authorities and consumers to draw significant conclusions about the value of audits in antimicrobial prescription intervention. Growing evidence[4] from recent larger studies suggests that such interventions are effective and improve patient care. An ASP with prospective audit and feedback was implemented in two surgical wards at our center. The aim of the audit was to improve the antibiotic management of surgical patients and to measure its impact on clinical outcomes and antimicrobial use.

METHODS

Study design and setting. We conducted a 20-month (January 2012 to October 2013) quasi-experimental study of the implementation of an ASP in two inpatient surgical wards at the Hospital del Mar, a 420-bed tertiary care teaching hospital in Barcelona, Spain, serving a population of up to 300,000 people. Patients were recruited from inpatients undergoing general and

vascular surgery.

Variables. Demographic variables were collected from each patient. The primary outcomes were the number of appropriate or inappropriate prescriptions and total days of hospital stay. The secondary objectives of the study included: total days of antibiotic administration and failure of treatment, the total number of recommendations made and adherence to them and 14-day and 30-mortality.

An antibiotic was considered to be inappropriately prescribed if it met one or more of the following criteria:

1. The empirical treatment choice was suboptimal according to microbiological results. 2. There were better alternatives (hospital antibiotic guidelines).

3. Wrong-dosage, duration of therapy, alternative route of administration.

Program setting

Description of the ASP. The ASP was set up as a multidisciplinary effort, with an ID specialist supported by a nurse, a clinical pharmacist and a clinical microbiologist. Consensus-building among surgical services in which the program was to be performed was achieved beforehand.

During the pre-intervention period (PI) (January-October 2012) the ID physician of the program retrospectively audited records for all prescribed antimicrobial agent(s) and assessed clinical indication(s), and clinical status. No recommendations were made during this period. After that, the intervention period (INT) (January-August 2013) started, following a prospective audit on antibiotic prescription model. The ID physician evaluated each patient on the 3rdday of antimicrobial therapy (allowing 72-h for bacterial cultures to be processed). In the event of inappropriate use (as previously defined) the recommendation was made on the same day, using a written form placed in the respective case notes and, whenever possible, by communicating directly with the prescriber. The potential recommendations were pre-specified and structured and the decision on the recommendation was taken by at least two ID physicians. Prescribers were not obliged to comply with the recommendations, so retaining autonomy over clinical decision-making. On the 7th day of antibiotic prescription, all participants were re-evaluated to assess the degree of compliance. No new recommendations were done that day.

A third review was carried out 30-days later, with an analysis of the clinical records to determine the clinical outcome of the episode.

Statistical Analysis. Qualitative variables were compared using the X^2 test or Fisher's exact test, and quantitative variables using the Student's t-test or the Wilcoxon rank sum test. A 2-tailed P value of 0.05 was used to determine statistical significance. A linear regression model was used to test for differences in selected outcome variables between the pre-intervention and intervention periods. This test controlled for age, sex, surgical department, the severity score (SAPS II) and anaesthetic risk score (ASA). The SATA v.13.0 package was used.

Ethics. The local Antimicrobial Sub-Committee and Ethical Committee approved this study. Informed consent from individual patients was waived since the ASP program constituted routine clinical practice and only anonymized data were analyzed.

RESULTS

We identified and included 298 patients who had been receiving antimicrobial therapy for at least 72 hours. We studied 141 (47%) patients (110 in the Department of General Surgery, 31 in Vascular Surgery) during the PI, and 157 (53%) patients (113 in General Surgery, 44 in Vascular Surgery) in the INT.

The baseline characteristics of the study population are summarized in table 1. Suspected or demonstrated infection was the reason for antimicrobial therapy in 282 (94%) audits. The most frequent indications for antimicrobial therapy were: intraabdominal infection in 93 (30%) cases (43 appendicitis (14%), 32 cholecystitis (10%), and 18 perforated colon cancer (6%)); 59 of urinary infection (20%); 38 skin and soft tissue infection (12%); and 30 respiratory infection (10%). There were no differences between both periods on these indications for antibiotic.

In the intervention period, treatment was considered appropriate in 97 (62%) audits with no recommendations made to change the prescribed antimicrobial regimen, whereas 59 (38%) audits recommended changing the antimicrobial

Table 1 Baseline characteristics of studied patients.

	Pre intervention period (PI)	Intervention period (INT)	p value
Patients, n	141	157	
Male, n (%)	97 (68%)	107 (61%)	0.84
Age in years, means (±SD)	64 (±20)	64(±15)	0.89
SAPS II (±SD)	26.4 (±10)	25.8 (±9.8)	0.95
Antimicrobials			
Amoxicillin-clavulanate	63 (44%)	55 (39%)	0.123
Cefotaxime	26 (18%)	41 (26%)	0.18
Ciprofloxacin	14(9%)	16(10%)	0.110
Piperacillin-tazobactam	13 (9%)	33(21%)	0.102
ASA V n(%)	2 (1.5%)	0 (0%)	n.s.
No ASA	37 (26.5%)	62 (39.5%)	0.22

SAPS II: simplified acute physiology score; ASA: anaesthetic risk score.

Table 2 Comparison between the two periods

	Pre intervention period (PI)	Intervention period (INT)	P value
Inappropriate therapy n (%)	38 (26.9)	59 (37.5)	0.07
Deviation from the hospital's antibiotic guidelines without a valid reason n (%)	24 (17)	26 (16.5)	0.18
Wrong dosage n (%)	6 (4)	14 (9)	<0.05
Lack of antimicrobial coverage n (%)	8 (6)	9 (5)	0.124
Length of stay (Q1-Q3)	14.7 (7-16.5)	10.7 (6-13)	<0.05
Days before initiation of antibiotic (SD)	4.3 (2.4)	3.9 (2.7)	0.242
Total days of antibiotic treatment, mean (SD)	12 (4)	9 (3.6)	0.007
Mortality			
Overall mortality (30-day mortality), n (%)	9 (6)	3 (2.2)	0.09
Related mortality (14-day mortality), n (%)	4 (3)	1 (1)	0.14

prescription. Nine (5 %) audits recommended discontinuation of all antimicrobial therapy in this second period.

Thirty-eight (26.9%) treatments in the PI period and 59 (37.5%) in the INT period were considered inappropriate (p=0.07). The most frequent reasons for inappropriate treatment were: deviating from the hospital's antibiotic guidelines without a valid reason, for 24 (17%) patients in the PI, 26 (16.5%) in the INT period (p=0.18); the wrong dosage, 6 (4%) patients in the PI, 14 (9%) in the INT (p=0.032); lack of antimicrobial coverage, 8 (6%) patients in the PI and 9 (5%) in the INT period (p=0.124) (table 2).

Fifty-five (93%) of the recommendations issued during the intervention period were complied with. The recommendation for 9 (5%) patients in the INT period was to increase the spectrum of the empiric antimicrobial therapy.

The mean (inter-quartile range Q1-Q3) length of stay (LOS) was 14.7 (7–16.5) days in the first period and 10.7 (6–13) days in the intervention period (p<0.005). LOS prior to the start of antimicrobial therapy, and so prior to the intervention, was not significantly different between the two periods (4.3±2.4 days in the PI and 3.9±2.7 days in the INT p=0.2). The total number of days receiving antimicrobial therapy was significantly higher in the PI period (12 days ± 4) compared with the intervention period (9 days ±3.6, p=0.007).

Twelve (4%) patients in all died (14-day mortality) during the study period: 9 (6.3%) in the first period and 3 (2%) in the second (p=0.09).

DISCUSSION

We report a significant reduction in the number of days of antimicrobial therapy and LOS, with no significant differences in mortality after implementing an antimicrobial stewardship program in two surgical wards at a tertiary care hospital. In previous studies, reductions in LOS were less significant[4-8] and differences of mortality were also not found. The evidence compiled from meta-analyses suggests that clinical outcomes are better, when there is an ASP[4]. Consistent with this, our report shows that the intervention had a direct impact on antimicrobial prescription, with a significant improvement in LOS and total days of antimicrobial therapy. In our study, the two periods were remarkably comparable, not only in the number of patients enrolled, but also in terms of gender, age and baseline condition severity. At the same time, the patients were in the same hospital and the same wards (same nurses, same rooms and so on). Moreover, it was the same investigator doing the assessment of the prescription (in the pre intervention and the intervention period) in order to protect against biased outcome assessment, although recommendation decision were consensuated between at least two ID physicians. According to the results, most of the initial prescriptions made by the surgeons were adequate. The most difficult cases with uncontrolled infectious sources or multidrug-resistant bacteria were those that benefited most from the ASP intervention.

In 9 cases in the intervention period, it was necessary to recommend increasing the spectrum of the prescribed antimicrobial and using more expensive antibiotics. The ultimate objective of the study was to improve clinical outcomes without overlooking improvements in antimicrobial management, which is why we believe that the participation of an ID specialist in an intervention can help optimize the management of antimicrobial therapy.

This study is similar to that by Nowak et al.[5], although they found no differences in LOS or mortality. In comparison with other hospitals, the number of initially inappropriately treated patients in our hospital was similar to those published in a recent meta-analysis by Kariv et al., who reported a pooled estimate rate of 28.65% for inappropriate treatment drawn from a wide range ofvery different studies[9].

There are limitations to our study. The first is that this is a single center study with a somewhat reduced sample size, which means that our results may not apply to other hospitals with a more restricted antimicrobial policy. Secondly, there is a potential misclassification bias because the outcomes could have been measured differently in the pre and post periods (since one period is retrospective and the intervention prospective). Probably performing an interrupted time series analysis, or at least plotting these outcomes over multiple timepoints could have protected against temporal confounding

and regression to the mean. Although we tried to avoid this bias by using the same investigator doing the evaluations in both periods. On the other hand, the strengths of our study include its prospective nature and the fact that the patients studied in both periods were similar and comparable.

In summary, we found that the implementation of an ASP in our hospital led to a significant reduction in LOS and the total duration of antimicrobial therapy in Surgical Wards. In addition, the ASP plays an integral role in providing guidance to non-ID specialists and ensures that appropriate antimicrobial agents are used.

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